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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/892505
Filing Date: 06/28/2001
Appellant(s): Kivlighn et al.

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EXAMINER'S ANSWER

This is in response to the appeal brief filed on 08/07/2008.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments

The appellant's statement of the status of amendments contained in the brief is correct.

(5) Summary of claimed subject matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

Grounds of Rejections to be Reviewed on Appeal:

1) Rejection of claims 16-17 under 35 U.S.C. 103(a) as being unpatentable over Maeda et al. (5,747,495), in view of Nakamoto et al. (EP 0 337 350), and further in view of applicant's admission.

2) Rejection of claim 18 under 35 U.S.C. 103(a) as being unpatentable over Baldwin (US 4,058,614), in view of Baldwin et al. (US 4,032,522).

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied upon

US 5,747,495	Maeda et al.	May 1998
EP 0 337 350	Nakamoto et al.	October 1989
US 4,058,614	Baldwin	November 1977
US 4,032,522	Baldwin	June 1977

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maeda et al. (5,747,495, PTO-892), in view of Nakamoto et al. (EP 0 337 350, PTO-1449), and further in view of applicant's admission.

Maeda et al. discloses a method of treating hypertension comprising administering to a patient in need thereof a therapeutically effective amount of a uric acid lowering agent, a xanthine oxidase inhibitor, 4-amino-6-hydroxypyrazolol [3,4-d]pyrimidine (AHPP). See abstract; column 2, lines 11-13; column 6, Example 9, claim 1. For oral administration of AHPP, the effective antihypertensive amount is 100-9000 mg/day/adult patient. See column 2, lines 63-65. It is also taught that uric acid production was inhibited by AHPP in a dose dependant manner i.e xanthine oxidase inhibitor lowers uric acid in a dose dependent manner. See column 4, Example 5.

Maeda et al. do not explicitly teach the administration of a therapeutically effective amount of xanthine oxidase inhibitor to achieve a uric acid level in the patient of 4 to 6 mg/dl in treating hypertension.

Maeda et al. do not teach administration of a therapeutically effective amount of allopurinol to achieve a uric acid level in the patient of 4 to 6 mg/dl in treating hypertension.

Nakamoto et al. teaches that compounds that lower uric acid are effective in treating hypertension. Nakamoto et al. also teaches that allopurinol is a well known agent employed to lower uric acid. Further, Applicant acknowledges that uric acid was known as a possible risk factor for hypertension. See instant specification page 2, lines 10-11.

It would have been obvious to a person of ordinary skill in the art to determine the optimal parameters such as effective amounts of xanthine oxidase inhibitor needed to achieve desired results i.e uric acid level in the patient of 4 to 6 mg/dl in treating

hypertension because 1) Maeda et al. teaches that uric acid production was inhibited by xanthine oxidase inhibitor, AHPP in a dose dependent manner, 2) Nakamoto et al. teaches that compounds that lower uric acid are effective in treating hypertension, and 3) Applicant acknowledges that uric acid was known as a possible risk factor for hypertension. Accordingly, one of ordinary skill in the art at the time of invention would have been motivated to optimize the amount of uric acid lowering agents, xanthine oxidase inhibitors to achieve uric acid levels of 5.0-6.9 mg/dL with reasonable expectation of success of treating hypertension, since as discussed above and further applicant also acknowledges that uric acid was known as a possible risk factor for hypertension.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer therapeutically effective amount of allopurinol to achieve a uric acid level in the patient of 4 to 6 mg/dl in treating hypertension.

One of ordinary skill in the art at the time of invention would have been motivated to administer allopurinol with reasonable expectation of success of treating hypertension by lowering uric acid because 1) applicant acknowledges that uric acid was known as a possible risk factor for hypertension and 2) Nakamoto also teaches that uric acid lowering agents are known to treat hypertension, and allopurinol is a uric acid lowering agent.

Further, the optimization of amounts of known agents to be administered to achieve a desired effect is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

Furthermore, it is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233,235 (CCPA 1955.)

It is pointed out that xanthine oxidase inhibitor, inhibits the conversion of xanthine to uric acid, i.e xanthine oxidase inhibitor when employed for treating hypertension reduces uric acid levels in the patient. Maeda et al. also exemplifies that uric acid production was inhibited by xanthine oxidase inhibitor AHPP in a dose dependent manner. Thus, the methods as taught by Maeda et al. necessarily result in reducing uric acid levels as recited in the claims, when the amount of AHPP are modified to achieve desired therapeutic effects

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Baldwin (US 4,058,614, PTO-892 of record), in view of Baldwin et al. (US 4,032,522, PTO-892 of record).

Baldwin '614 teaches a method of treating hypertension comprising administering xanthine oxidase inhibitor. See abstract; Column 1, lines 21-31.

Baldwin does not teach the particular xanthine oxidase inhibitor, allopurinol in the method therein.

Baldwin et al. '522 teaches that allopurinol acts as a specific inhibitor of the enzyme xanthine oxidase which is responsible for the conversion of hypoxanthine and xanthine to uric acid. See column 1, lines 54-60. Baldwin et al. discloses a method of reducing uric acid in a patient by administering xanthine oxidase inhibitors, trifluoromethylimidazoles. See abstract; column 2. It is also disclosed that the compounds therein are anti-hyperuricemic agents, and exhibit anti-hypertensive activity. See column 5, lines 36-45; column 6, lines 5-52.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer allopurinol in the method of treating hypertension because 1) Baldwin '614 teaches that xanthine oxidase inhibitors are useful in treating hypertension, and 2) Baldwin et al. '522 teach that allopurinol acts as a specific inhibitor of the enzyme xanthine oxidase. Accordingly, one of ordinary skill in the art at the time of invention would have been motivated to administer allopurinol with reasonable expectation of success of treating hypertension, since Baldwin et al. '522 teach allopurinol to be functionally equivalent as xanthine oxidase inhibitor.

(10) Response to Argument

1) Rejection of claims 16-17 under 35 U.S.C. 103(a) as being unpatentable over Maeda et al. (5,747,495, PTO-892), in view of Nakamoto et al. (EP 0 337 350, PTO-1449), and further in view of applicant's admission, should be affirmed.

Appellant argues that "nowhere in the Maeda et al. reference can it be reasonably said that Maeda et al. suggests that uric acid causes hypertension and that controlling uric acid serves to treat hypertension." See page 4, of the Brief.

In response, it is pointed out that appellant is arguing against a single reference when the rejection was based on combination of references. Maeda et al. teaches employment of xanthine oxidase inhibitors such as AHPP in the treatment of hypertension. Maeda et al. also teaches that uric acid production by xanthine oxidase was inhibited by AHPP in a dose-dependent manner. Nakamoto et al. teaches that compounds that lower uric acid are effective in treating hypertension. Further, Applicant acknowledges that elevated uric acid confers an increased risk for the development of hypertension. See instant specification page 2, lines 10-11. From the teachings of Nakamoto et al., and Applicant's acknowledgement that uric acid was known as a possible risk factor for hypertension, one would have recognized uric acid levels as result effective parameter/variable in treating hypertension. Maeda et al. teaches that uric acid production was inhibited by xanthine oxidase inhibitor, AHPP in a dose dependent manner i.e levels of uric acid can be optimized by adjusting the amounts of xanthine oxidase inhibitor, AHPP. Accordingly, one of ordinary skill in the art at the time of invention would have been motivated to optimize the amount of uric acid lowering agents, xanthine oxidase inhibitors to achieve desired uric acid levels of 5.0-6.9 mg/dL with reasonable expectation of success of treating hypertension, since as discussed

above and further applicant also acknowledges that uric acid was known as a possible risk factor for hypertension. Further, the optimization of amounts of known agents to be administered to achieve a desired effect is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

Appellant argues that "Dr. Rodriguez-Iturbe clarifies that Maeda et al. does not suggest that the transient lowering of blood pressure by AHPP is due to uric acid, but rather was due to oxidative stress." See page 5, of the Brief.

In response, it is pointed out that Maeda et al. reference was employed for its teaching that xanthine oxidase inhibitors such as AHPP are useful in treating hypertension.

Appellant argues that "Applicant has provided expert evidence and related prior art references which establish that no expectation of successfully treating hypertension by lowering uric acid existed at the time of filing the present application." See page 7, of the Brief.

In response, it is pointed out that Nakamoto et al. clearly teaches that compounds that lower uric acid are effective in treating hypertension, and Applicant also acknowledges in the instant specification that uric acid was known as a possible risk factor for hypertension. Accordingly, one of ordinary skill in the art at the time of invention would be motivated to optimize the amounts of xanthine oxidase inhibitor to achieve uric acid levels of 5.0-6.9 mg/dL with reasonable expectation of success of treating hypertension, since as discussed above and further applicant also acknowledges that uric acid was known as a possible risk factor for hypertension.

Appellant argues that "The Nakamoto et al. reference discloses a new uricosuric agent, as opposed to a xanthine oxidase inhibitor for the purpose of treating hyperuricemia (gout). Thus, the Nakamoto et al. reference relates to an entirely different type of compound." See page 8, of the Brief.

In response, it is pointed out that both uricosuric agent, and xanthine oxidase inhibitor reduce the amount of uric acid in plasma. Nakamoto clearly teaches that compounds therein that lower uric acid are effective in treating hypertension, and the compounds that lower uric acid include uricosuric compounds, and also xanthine oxidase inhibitors because Nakamoto et al. provides examples of xanthine oxidase inhibitors such as allopurinol, benzbromarone, probenecid as uric acid lowering agents. Accordingly, there is clear motivation to employ uric acid lowering agents to treat hypertension, since as discussed above and further applicant also acknowledges that uric acid was known as a possible risk factor for hypertension.

Appellant argues that "The declarations of Drs. Johnson and Weir prove that the statement made in the Nakamoto patent relied on by the Examiner is so flawed that it would not be given any weight, and indeed was not given weight by those skilled in the art.....In fact, the evidence surrounding the Nakamoto patent reveals that the Nakamoto patent was never accepted by those skilled in the art as teaching a treatment of hypertension Dr. Weir goes on to explain". See pages 8-9, of the Brief.

Appellant's arguments have been considered, but not found persuasive. Nakamoto et al. clearly teaches that compounds that lower uric acid are effective in treating hypertension, and Applicant also acknowledges in the instant specification that uric acid was known as a possible risk factor for hypertension. Further, appellant admits in the Brief (see page, bottom paragraph of the Brief) that the association of uric acid

with hypertension has been known since their early work. Accordingly, one of ordinary skill in the art at the time of invention would have been motivated to target uric acid levels by optimize the amounts of xanthine oxidase inhibitor to achieve uric acid levels of 5.0-6.9 mg/dL with reasonable expectation of success of treating hypertension.

2) Rejection of Claim 18 under 35 U.S.C. 103(a) as being unpatentable over Baldwin (US 4,058,614), in view of Baldwin et al. (US 4,032,522) should be affirmed.

Appellant argues that "Baldwin does not connect the inhibition of xanthine oxidase with the lowering of blood pressure, and in fact suggests that the inhibition of xanthine oxidase and the lowering of blood pressure involved different imidazole compounds." See page 11, of the Brief.

In response, it is pointed out that contrary to Appellant's assertion that "inhibition of xanthine oxidase and the lowering of blood pressure involved different imidazole compounds", Baldwin '614 teaches same compounds as inhibitors of xanthine oxidase, and as antihypertensive agents. See column 8, claim 7; column 9, claim 14 wherein the same substituted imidazole compounds are useful as xanthine oxidase inhibitors and antihypertensive agents. Accordingly, the substituted imidazole compounds which are xanthine oxidase inhibitors are useful in lowering blood pressure i.e Baldwin '614 teaches a method of treating hypertension comprising administering substituted imidazole compounds which are xanthine oxidase inhibitors.

Appellant argues that "Baldwin does not reference allopurinol which is a xanthine oxidase inhibitor and not an imidazole, nor does he relate the lowering of blood pressure with a target uric acid level." See page 11, of the Brief.

In response, it is pointed out that applicant is arguing against a single reference when the rejection was based on combination of references. Further, Baldwin '614 need not relate the lowering of blood pressure with a target uric acid, since claim 18 does not address this limitation.

Appellant argues that "There is no suggestion to modify the Baldwin et al. reference to somehow concoct a method of treating hypertension by administering allopurinol. Furthermore, substantial evidence provided by the Applicants establishes that even if such modification to the Baldwin et al. reference were made, there would have been no reasonable expectation of successfully treat hypertension by administering allopurinol." See page 12, of the Brief.

In response, Baldwin '614 teaches compounds therein as inhibitors of xanthine oxidase, and as antihypertensive agents. Baldwin '614 teaches a method of treating hypertension comprising administering substituted imidazole compounds therein which are xanthine oxidase inhibitors. See column 1, lines 53-68. Baldwin et al. '522 teaches that allopurinol acts as a specific inhibitor of the enzyme xanthine oxidase which is responsible for the conversion of hypoxanthine and xanthine to uric acid. It would have been obvious to a person of ordinary skill in the art at the time of invention to administer allopurinol in the method of treating hypertension because 1) Baldwin '614 teaches that substituted imidazole compounds therein which are xanthine oxidase inhibitors are useful in treating hypertension, and 2) Baldwin et al. '522 teach that allopurinol acts as a specific inhibitor of the enzyme xanthine oxidase. Accordingly, one of ordinary skill in the art at the time of invention would have been motivated to administer allopurinol with reasonable expectation of success of treating hypertension, since Baldwin et al. '522

teach allopurinol to be functionally equivalent as xanthine oxidase inhibitor, and xanthine oxidase inhibitors are known to treat hypertension.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a).

(11) Related Proceedings Appendix
None

Respectfully submitted,

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Conferees

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